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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,643	01/10/2002	Nigel C. Phillips	02811-0161US	2086

23370 7590 03/10/2004

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/937,643	PHILLIPS ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-50 and 66-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-50 and 66-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date SEE ATTACHED
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 12/8/03. The amendment has been entered. Claims 40, 48 and 66-68 have been amended. New claims 69-78 have been added. Claims 26-50 and 66-78 are currently pending in the application and are examined herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 26-56 and 66-68 remain rejected, and new claims 69-78 are now rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-30 of U.S. Patent No. 6,326,357 (hereafter '357) in view of Morales (Journ. Urology, Vol. 153, p. 1706-1710, 1995), for the reasons of record.

5. Additionally, claims 26-56 and 66-68 remain rejected, and new claims 69-78 are now rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-30 of U.S. Patent No. 6,329,347 (hereafter '347) in view of Morales (Journ. Urology, Vol. 153, p. 1706-1710, 1995), for the reasons of record.

6. It is noted that new claims 69-78 are drawn to methods of treating prostate cancer comprising administering a composition comprising M-DNA obtained from a disrupted mycobacterium using DNAse-free reagents and a pharmaceutically acceptable carrier to an animal or human having prostate cancer in an amount to have an antineoplastic effect on the prostate cancer.

7. As indicated in the previous Office Action, US Patent No. 6,326,357 (hereafter '357) teaches methods of treating cancer in a patient having cancer by administering a composition comprising: a) mycobacterial DNA obtained from a disrupted mycobacterium using DNAse-free reagents, and b) a pharmaceutically acceptable carrier to an animal or human having cancer. Similarly, US Patent No. 6,329,347 (hereafter '347) teaches methods of treating bladder cancer in a patient having cancer by administering a composition comprising: a) mycobacterial DNA obtained from a disrupted mycobacterium using DNAse-free reagents, and b) a pharmaceutically acceptable carrier to an animal or human having cancer. Neither the '357 or '347 reference specifically teaches that the composition can be used to treat prostate cancer. However, Morales teaches a similar mycobacterial composition, a mycobacterial cell wall complex, can be used to treat prostate cancer. Furthermore, data disclosed in '357 and '347 indicates that it is the DNA component of the mycobacterial cell wall composition that is the critical element for the anti-

cancer effects. Specifically, both '357 and '347 teach that cancer cells treated with the mycobacterial cell wall complex or with mycobacterial DNA purified from the cell wall complex could inhibit cancer cell proliferation and induce apoptosis in the cancer cells. Furthermore, treatment of mycobacterial cell wall complex and the DNA isolated from the cell wall complex with DNAse destroyed the anti-cancer effects (see Examples 17 and 18 columns 19-21 of '357; and, Examples 6 and 7, columns 13-14 of '347). Therefore, it is clear that the anticancer effects are due to the mycobacterial DNA component of the composition. Since, Morales indicates a mycobacterial cell wall composition that has anti-cancer effects, it would be prima facie obvious to one of ordinary skill in the art at the time of filing that the mycobacterial cell wall complex of Morales MUST comprise mycobacterial DNA. Since Morales teaches that the mycobacterial cell wall complex has anti-prostate cancer it also would have been prima facie obvious to one of ordinary skill in the art at the time of filing that the mycobacterial compositions of '357 and '347 could be used to treat prostate cancer with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to combine the teachings of the '357 and '347 Patents with Morales because Morales teaches treating prostate cancer with a similar mycobacterial composition. Therefore, one of ordinary skill in the art would have been motivated to treat prostate cancer with the mycobacterial compositions taught in the '357 and '347 references with a reasonable expectation of success.

Response to Arguments

8. Applicant's arguments filed 12/8/03 have been fully considered but they are not persuasive.

9. Applicants argue that neither the '357 or the '347 Patents teach treatment of prostate cancer and that Morales does not teach anti-cancer composition comprising mycobacterial (M. phlei) DNA. Additionally, applicants argue that Morales cannot be properly combined with either the '357 or '347 patents because the Morales composition is distinct from the compositions disclosed in the indicated patents.

10. In response, applicants' arguments have been fully considered, but they are not persuasive.

11. First, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

12. Second, in response to applicants argument that Morales cannot be properly combined with the other references because the Morales composition is distinct from the '347 or '357 compositions, the Examiner respectfully disagrees because all of the references teach mycobacterial compositions that have anti-cancer effects when administered to cancer cells. As indicated in the previous Office Action, the '347 and '357 Patents teach mycobacterial compositions that can be used to treat cancer, including mycobacterial cell wall complexes as well DNA isolated from the mycobacterial cell wall. The '347 and '357 patents do not indicate that the mycobacterial compositions can be used to treat prostate cancer. However, Morales teaches a mycobacterial composition that can treat prostate cancer. Applicants argue that the Morales mycobacterial composition is distinct from the compositions of the '347 and '357 Patents. Considering that Morales teaches that mycobacterial cell wall complex can treat prostate

cancer, and also considering that the '347 and '357 patents teach compositions comprising or derived from mycobacterial cell wall complexes that can treat cancer, it is the opinion of the Examiner that the compositions are not functionally distinct. Furthermore, since the '347 and '357 patents teach that the component that confers the anti-cancer effect to the mycobacterial compositions is the mycobacterial DNA, it would have obvious to one of ordinary skill in the art that the mycobacterial complex used by Morales MUST comprise mycobacterial DNA, since it has anti-cancer activity. Therefore, since the mycobacterial complex of Morales is effective at treating prostate cancer and is not functionally distinct from the mycobacterial complexes taught by the '347 and '357 patents, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to use any of the anti-cancer compositions of '357 or '347 to treat prostate cancer. Therefore, the rejection is not withdrawn.

Claim Rejections - 35 USC § 112, first paragraph

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 26-56 and 66-68 remain rejected and new claims 69-78 are now rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> Methods for inhibiting prostate tumor growth comprising the administration of a composition comprising:
>
> (a) mycobacterial DNA obtained from a disrupted mycobacterium using DNase-free reagents in order to at least partially preserve the DNA; and,

(b) a pharmaceutically acceptable carrier

to an animal or human harboring a prostate tumor, wherein said composition is directly delivered to said prostate tumor in an amount effective to inhibit the growth of said prostate tumor.

Does not reasonably provide enablement for the full scope encompassed by the claims. Specifically, the claims are not enabled for general delivery (i.e., any route of administration other than direct delivery to the prostate tumor, such as systemic delivery) of the claimed composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Response to Arguments

15. Applicant's arguments filed 12/8/03 have been fully considered. Applicants' arguments with respect to the administration of any type of mycobacterial DNA (not just M. phlei DNA) is persuasive. However, Applicants' arguments with respect to any type of administration other than direct administration to the prostate tumor are not persuasive.

16. Applicants argue that the specification has support for the various routes of administration encompassed by the claims (see page 15 of the response). Applicants also direct the Examiner to Examples 5-7 of the specification, and argue that given the substantial experimental data supporting the role of the present invention in inhibiting prostate cancer cell proliferation, one skilled in the art would be able to readily extrapolate the analogous applicability of these findings to administering the compositions via the blood stream to the prostate cancer site (see p. 15).

In response, it is respectfully pointed out that Examples 5-7 involve the treatment of cancer cells *in vitro* (i.e., in a cell culture dish) which is not analogous to general delivery through the bloodstream, but is analogous with direct delivery to the prostate tumor. Furthermore, as indicated in the previous Office Action, Morales explicitly teaches, "successful immunotherapy of solid neoplasms has been an elusive goal" (see p1706, first paragraph). Morales teaches that although administration of mycobacteria phlei cell wall (MCW) by intratumoral administration results in regression of established prostate tumors, "the response, however, depends initially on the route of administration. The intraperitoneal route was found to be not only in effective, but detrimental" (See p. 1709, bottom, first column); and, "[T]he intraperitoneal administration of MCW did not alter tumor-growth kinetics... the rats receiving MCW by this route became lethargic, anorexic and exhibited considerable hair loss." (See p. 1707, middle of first column). Thus, indicating that only administration of the mycobacterial compositions directly to the prostate tumor has been shown to be effective for inhibiting the tumor growth. Furthermore, as previously indicated, the examples disclosed in the specification do not indicate any routes of administration other than direct delivery to the prostate tumor that actually result in an anti-tumor effect. That is, there is no evidence presented that clearly indicates the mycobacterial compositions can be administered intravenously (or any other route other than direct delivery to the tumor) and result in the anti-cancer effects. Therefore, the rejection is not withdrawn. It is noted, however, that limiting the claims to administering the mycobacterial compositions directly to the prostate tumor would obviate this rejection.

Miscellaneous

The rejection of claims under 35 U.S.C. 112, second paragraph have been obviated in view of the amendments to the claims.

Conclusion

17. No claim is allowed.

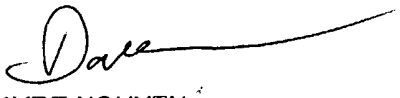
18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action (i.e., the rejection of the newly added claims). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



DAVE T. NGUYEN
PRIMARY EXAMINER

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Art Unit 1635